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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/831,458	05/08/2001	Y. Tom Tang	PF-0636 USN	4361

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EXAMINER
O HARA, EILEEN B

ART UNIT	PAPER NUMBER
1646	15

DATE MAILED: 01/15/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/831,458	TANG ET AL.	
	Examiner	Art Unit	
	Eileen B. O'Hara	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 October 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-42* is/are pending in the application.

4a) Of the above claim(s) *32-34 and 38-42* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-31 and 35-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *21-42* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *13* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Claims 21-40 are pending in the instant application. Claims 1-20 have been canceled and claims 21-40 have been added as requested by Applicant in Paper Number 14, filed Oct. 21, 2002.

Election/Restrictions

2. Applicant's election with traverse of Group A, corresponding to newly added claims 21-32 and 35-37, in Paper No. 12 is acknowledged.

Applicants submit that newly added claims 32-34, 38-40, 41 and 42 should be examined together with claims 21-31 and 35-37, and request that upon allowance of the claims drawn to the polynucleotides and polypeptides these claims be rejoined. If the claims drawn to polynucleotides and polypeptides are found allowable, claims 32-34, 38-40, 41 and 42 will be rejoined if they encompass the same scope.

Applicant's traversal to elect one polypeptide and its encoding polynucleotide, (SEQ ID NOS: 12 and 25) is acknowledged. The traversal is on the ground(s) that the polynucleotide and polypeptide sequences of SEQ ID NOS: 1-26 are written so that the sequences are part of a Markush group, and that these Markush groups are proper. Applicants submit that if the members of the Markush group are sufficiently few in number or so closely related that a search and examination of the entire claim can be made without serious burden, the examiner must examine all claims on the merits, even though they are directed to independent and distinct inventions. Applicants also submit that it is improper for the Office to refuse to examiner that

which applicants regard as their invention, unless the subject matter in a claim lacks unity of invention, and that the polypeptides and polynucleotides of the instant invention share a common utility in, for example, toxicology studies based on expression profiling.

This is not found persuasive because consistent with current patent practice, a serious search burden may be established by (A) separate classification thereof: (B) a separate status in the art when they are classifiable together: (C) a different field of search:. These criteria were met in the above restriction. For example, though the 13 polynucleotides and encoded polypeptides are classified in the same class and subclass, are distinct inventions because they are drawn to different nucleic acid sequences encoding different proteins having different structures and functions and would require separate searches and consideration, and as stated in the MPEP § 803, "a serious burden on the examiner may be *prima facie* shown if the examiner shows by appropriate explanation either separate classification, separate status in the art, or a different field of search as defined in MPEP § 808.02.". The polynucleotides and polypeptides would require separate sequence searches, so that the Office would have to search several different databases for 26 separate sequences, which would be a serious burden on the examiner and the office, especially considering the enormous numbers of sequences currently deposited in the sequence databases, which is continuing to grow at a logarithmic rate. Thus, to search all inventions would be burdensome. Applicants' arguments that the polynucleotides and polypeptides of the invention share a common utility in toxicology studies based on expression profiling is also is not found persuasive. Any expressed polynucleotide and polypeptide can be used in such a method, so that there is no shared special technical feature. The different polynucleotides and polypeptides do not share a common utility.

The requirement is still deemed proper and is therefore made FINAL.

Claims 32-34 and 38-40 are withdrawn as being drawn to a non-elected invention.

Claims 21-31 and 35-37 are currently under examination, and will be examined in so far as they pertain to nucleic acids and protein of HCSRP-12.

Information Disclosure Statement

3. The sequences disclosed in the IDS filed Oct. 21, 2002 (references 1 and 2) have been considered to the extent that was possible absent an explanation of relevance or a sequence alignment.

Priority

4. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) as follows: An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification (37 CFR 1.78).

Claim Objections

5. Claims 21, 22, 25, 29, 30 and 36 are objected to as reciting an improper Markush Group. M.P.E.P. 803.02 states that:

"Since the decisions in In re Weber **,198 USPQ 328 (CCPA 1978); and In re Haas, 198 USPQ 334 (CCPA 1978), it is improper for the Office to refuse to examine that which applicants regard as their invention, unless the subject matter in a claim lacks unity of invention, In re Harnish , 631 F.2d 716, 206 USPQ 300 (CCPA 1980); Ex Parte Hozumi , 3 USPQ2d 1059

(Bd. Pat. App. & Int. 1984). Broadly, unity of invention exists where compounds included within a Markush group (1) share a common utility and (2) share a substantial structural feature disclosed as being essential to that utility."

The claims recite compounds drawn to non-elected SEQ ID NOS which should be deleted.

Appropriate correction is required.

Claim Rejections - 35 USC § 101 and § 112

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

6. Claims 21-31 and 35-37 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial utility or a well established utility.

Claims 21-31 and 35-37 are directed to isolated nucleic acid molecules comprising the nucleotide sequence of SEQ ID NO: 25 and the encoded protein having the amino acid sequence shown in SEQ ID NO: 12, identified as human cell surface receptor protein-12 (HCSRP-12), and methods of treatment comprising administering the protein. The instant specification teaches that this protein is a cell surface receptor, based on the presence of a putative secretory signal sequence, transmembrane domain and homology to a known receptor, Non-CD4 glycoprotein pg120 receptor. However, there is no activity attributed to the protein, no teaching of any specific disease or disorder correlated with the protein and no disclosure of any protein or molecule (such as a ligand) that interacts with it. Therefore, the nucleic acid, encoded protein and methods of use do not have any specific and substantial utility, or a well established utility,

as determined according to the current Utility Examination Guidelines, Federal Register, Vol. 66, No. 4, pages 1092-1099, Friday, January 5, 2001.

The instant specification teaches that the gene is expressed in hematopoietic/immune tissue, gastrointestinal, cardiovascular, endocrine, nervous and reproductive tissues (Table 3, column 3), and column 4 of Table 3 lists diseases, disorders or conditions associated with those tissues (inflammation, fetal (development) and trauma). The specification also asserts that the nucleic acid molecules, encoded protein, and antibodies (agonists or antagonists) may be use in diagnostic and therapeutic applications, and provides an extensive list of diseases and disorders on pages 31-33 and 40-43. However, there is no nexus between any of the disorders and the molecules of the instant invention. Additionally, the specification also asserts that HCSRP may be used to diagnose or treat the listed diseases, but specification also includes twelve other genes encoding polypeptides that are named HCSRP, all of which are structurally and functionally different genes and encoded proteins (Table 2) that are expressed in different tissues (Table 3). Therefore the asserted use for diagnosis or treatment of these diseases is not specific and substantial. Also, a stated belief that a correlation exists between the nucleic acids (polypeptides) and the above diseases and disorders, based on tissue expression alone, is not sufficient guidance to use the claimed polynucleotides or proteins to treat and/or diagnose a particular disease; it merely defines a starting point for further research and experimentation. There is no RFLP polymorphism disclosed for this gene, or any other type of alteration that would result in a change in structure or expression, so the use of the HCSRP-12 gene as a diagnostic or prognostic marker is conjectural and would not, on the basis of the disclosure, be considered useful by one of skill in the art.

The instant application has failed to provide guidance as to how one of skill in the art could use the claimed invention in a way that constitutes a specific or substantial utility. The proposed uses of the claimed invention are simply starting points for further research and investigation into potential practical uses of the claimed nucleic acids and protein.

The instant application also teaches that the molecules of the invention can be used to determine function of the protein (pages 54-55), screen for antagonists or agonists, orthologs, allelic variants, screen for molecules that bind to the polypeptide, and that the nucleic acids can be used to recombinantly produce protein, detect nucleic acid expression, and the protein can be use to generate antibodies. However, these are considered to be general uses or methods that would also apply to any nucleic acid and/or protein, and are not specific to the nucleic acids or protein of the instant invention.

In Brenner v. Manson, 148 U.S.P.Q. 689 (sus. Ct., 1966), the court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad definition was not the intended definition of "useful" as it appears in 35 U.S.C. 101, which requires that an invention must have either an immediately obvious or fully disclosed "real world" utility. The instant claims are drawn to polynucleotides and encoded protein which have undetermined function or biological significance, and the use of a protein to discover its properties does not constitute a specific, substantial utility. All of the biological activities of a protein need not be known to obtain a patent, but there must be at least one specific and substantial activity or function known. It is possible that, after further characterization, the HCSRP-12 nucleic acid molecules or proteins might be found to be associated with a specific disease, in which case they would have a

patentable utility. This further characterization, however, is part of the act of invention and until it has been undertaken the Applicant's claimed invention is incomplete.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7.1 Claims 21-31 and 35-37 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. Even if the specification were enabling of how to use the HCSRP-12 nucleic acid or polypeptide, enablement would not be found commensurate in scope with the claims. If one of skill in the art does not know how to use the nucleic acids or proteins the skilled artisan would clearly not know how to use nucleic acids encoding and polypeptides that are 90% identical to the amino acid sequence of SEQ ID NO: 12, or fragments of SEQ ID NO: 12 or polynucleotides comprising at least 60 contiguous nucleotides of SEQ ID NO: 25.

7.2 Claims 21, 23, 26, 27, 28, 30, 31, 35 and 37 are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The specification describes apolynucleotide and encoded polypeptide having the sequences consisting of SEQ ID NOS: 25 and 12 . However, the claims as written include polynucleotides and polypeptides comprising

fragments and homologues, encompass polynucleotides and polypeptides that vary substantially in length and also in amino acid composition. The instant disclosure of one polypeptide does not adequately support the scope of the claimed genus, which encompasses a substantial variety of subgenera. A genus claim may be supported by a representative number of species as set forth in *Regents of the University of California v Eli Lilly & Co,* 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997), which states:

"To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention". Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1980) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed.") Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d 1565, 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id at 1170, 25 USPQ2d at 1606."

A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a

substantial portion of the genus. The instant specification discloses, however, only one polypeptide, with no disclosed activities. For example, Transforming Growth Factor (TGF-beta) Family OP-1 induces metanephrongenesis whereas closely related TGF-beta family members-BMP-2 and TGF-beta1-have no effect on metanephrogenesis under identical conditions (Vukicevic et al., 1996, PNAS USA 93:9021-9026). Platelet-derived Growth Factor (PDGF) Family VEGF, a member of the PDGF family, is mitogenic for vascular endothelial cells but not for vascular smooth muscle cells while PDGF is mitogenic for vascular smooth muscle cells but not for vascular endothelial cells (Tischer et al., U.S. Patent 5,194,596, column 2, line 46 to column 3, line 2). Finally, vertebrate growth hormone of 198 amino acids becomes an antagonist (inhibitor of growth) when a single amino acid is changed (Kopchick et al, U.S. Patent No. 5,350,836). Even 99% homology does allow predictability in this instance. Given the unpredictability of homology comparisons, and the fact that the specification fails to provide objective evidence that the additional sequences are indeed species of the claimed genus it cannot be established that a representative number of species have been disclosed to support the genus claim.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 21-31 and 35-37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims are rejected because the independent claims 21

and 30, recite a "naturally occurring" polypeptide or polynucleotide, and it is not clear what is meant by the term "naturally occurring".

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8.1 Claims 21, 23, 26, 27, 28 and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Curtis et al., Proc. Natl. Acad. Sci., U.S.A. Vol 89, pp.-8356-8360, 1992.

Claims 21, 23, 26, 27, 28 and 31 encompass an isolated polypeptide that is an immunogenic fragment of the polypeptide of SEQ ID NO: 12, isolated polynucleotide encoding the fragment which may be operably linked to a promoter sequence, method for producing the polypeptide, and an isolated polynucleotide comprising at least 60 contiguous nucleotides of a polynucleotide of SEQ ID NO: 25.

Curtis et al. discloses DNA encoding a polypeptide identified as gp120 receptor (Fig. 2) that is 82% identical to the polypeptide of SEQ ID NO: 12 of the instant invention (see attached sequence alignments). Curtis teaches making a peptide fragment of the gp120 receptor and immunizing rabbits to generate antisera. Curtis et al. teach cells transformed with a recombinant polypeptide comprising nucleic acids encoding the gp120 receptor or receptor fragment, recombinant production of protein, and the polynucleotide comprises more than 60 contiguous

nucleotides of the polynucleotide of SEQ ID NO: 25 of the instant invention. Therefore, Curtis et al. anticipates the claims.

9.2 Claim 23 and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Hillier et al., Database EST, Accession No. R98113, Sept. 11, 1995.

Claims 23, and 31 encompass isolated polynucleotide encoding and immunogenic fragment of SEQ ID NO: 12 and an isolated polynucleotide comprising at least 60 contiguous nucleotides of a polynucleotide of SEQ ID NO: 25.

Hillier et al. disclose a polynucleotide that comprises more than 60 contiguous nucleotides of the nucleic acid sequence of SEQ ID NO: 25, which would encode an immunogenic fragment of the polypeptide of SEQ ID NO: 12. Therefore, Hillier et al. anticipates the claims.

9.3 Claims 21, 23, 26, 27, 28, 31, 35 and 37 are rejected under 35 U.S.C. 102(a) as being anticipated by Kato et al., WO 98/55505, Dec. 10, 1998.

Claims 21, 23, 26, 27, 28, 31, 35 and 37 encompass an isolated polypeptide that is an immunogenic fragment of the polypeptide of SEQ ID NO: 12, isolated polynucleotide encoding the fragment which may be operably linked to a promoter sequence, method for producing the polypeptide, a composition comprising the polypeptide and a pharmaceutically acceptable excipient, method of treating a disease or condition comprising administering the polypeptide, and an isolated polynucleotide comprising at least 60 contiguous nucleotides of a polynucleotide of SEQ ID NO: 25.

Kato et al. discloses DNAs (SEQ ID NOS: 21 and 39, clone HP01263, pages 32-35)

encoding a polypeptide identified as being homologous to gp120-binding C-type lectin (SEQ ID NO: 3) that is 68% identical to the polypeptide of SEQ ID NO: 12 of the instant invention and 83% identical over 238 amino acids. The polynucleotide encoding the polypeptide comprises more than 60 contiguous nucleotides of the polynucleotide of SEQ ID NO: 25 of the instant invention (see attached sequence alignments). Kato et al. teaches making a peptide fragment of the polypeptide to generate antibodies, teaches cells transformed with a recombinant polypeptide comprising nucleic acids encoding the polypeptide or fragment, and recombinant production of protein (pages 6-7). Kato et al. also teaches that the polypeptide may be used as a pharmaceutical (page 56), and treatment of disorders or diseases comprising administering the polypeptide. Therefore, Kato et al. anticipates the claims.

Conclusion

10. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eileen B. O'Hara, whose telephone number is (703) 308-3312. The examiner can normally be reached on Monday through Friday from 10:00 AM to 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached at (703) 308-6564.

Official papers Before Final filed by RightFax should be directed to (703) 872-9306.

Official papers After Final filed by RightFax should be directed to (703) 872-9307.

Official papers filed by fax should be directed to (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Eileen B. O'Hara, Ph.D.

Patent Examiner

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